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MELANOMA AND TREATMENTS THEREOF

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MELANOMA AND TREATMENTS THEREOF

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PPPRPTAAARAPALGYKMAALSGGGGGGAEPGQALFNGDMEPEAGAGAGAAASSAADPAIPEEVWNIKQMIKLTQ EHIEALLDKFGGEHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPS SLSVFQNPTDVARSNPKSPQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPI GWDTDISWLTGEELHVEVLENVPLTTHNFVRKTFFTLAFCDFCRKLLFQGFRCQTCGYKFHQRCSTEVPLMCVNY DQLDLLFVSKFFEHHPIPQEEASLAETALTSGSSPSAPASDSIGPQILTSPSPSKSIPIPQPFRPADEDHRNQFG QRDRSSSAPNVHINTIEPVNIDDLIRDQGFRGDGGSTTGLSATPPASLPGSLTNVKALQKSPGPQRERKSSSSSE DRNRMKTLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKWHGDVAVKMLNVTAPTPQQLQAFKNEVGVLRKT RHVNILLFMGYSTKPQLAIVTQWCEGSSLYHHLHIIETKFEMIKLIDIARQTAQGMDYLHAKSIIHRDLKSNNIF LHEDLTVKIGDFGLATVKSRWSGSHQFEQLSGSILWMAPEVIRMQDKNPYSFQSDVYAFGIVLYELMTGQLPYSN INNRDQIIFMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKKRDERPLFPQILASIELLARSLPKIHRSASEPSL NRAGFQTEDFSLYACASPKTPIQAGGYGAFPVH

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AAARAPALGYKMAALSGGGGGGAEPGQALFNGDMEPEAGAGAGAAASSAADPAIPEEVWNIKQMIKLTQEHIEAL LDKFGGEHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQ NPTDVARSNPKSPQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPIGWDTDI SWLTGEELHVEVLENVPLTTHNFVRKTFFTLAFCDFCRKLLFQGFRCQTCGYKFHQRCSTEVPLMCVNYDQLDLL FVSKFFEHHPIPQEEASLAETALTSGSSPSAPASDSIGPQILTSPSPSKSIPIPQPFRPADEDHRNQFGQRDRSS SAPNVHINTIEPVNIDDLIRDQGFRGDGGSTTGLSATPPASLPGSLTNVKALQKSPGPQRERKSSSSSEDRNRMK TLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKWHGDVAVKMLNVTAPTPQQLQAFKNEVGVLRKTRHVNIL LFMGYSTKPQLAIVTQWCEGSSLYHHLHIIETKFEMIKLIDIARQTAQGMDYLHAKSIIHRDLKSNNIFLHEDLT VKIGDFGLATVKSRWSGSHQFEQLSGSILWMAPEVIRMQDKNPYSFQSDVYAFGIVLYELMTGQLPYSNINNRDQ VLCPPWEYNK

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 ${\tt FMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKKRDERPRLYLILASIELLARSLPKIHRSASEPSLNRAGFQTE} \\ {\tt DFSLYACASPKTPIQAGGYGAFPVH}$

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 $\label{thm:constraint} \textbf{AAARAPALGYKMAALSGGGGGGAEPGQALFNGDMEPEAGAGAGAAASSAADPAIPEEVWNIKQMIKLTQEHIEALLDKFGGEHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQNPTDVARSNPKSPQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGYGLYVT$

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 $\label{thm:constraint} AARAPALGYKMAALSGGGGGAEPGQALFNGDMEPEAGAGAAASSAADPAIPEEVWNIKQMIKLTQEHIEALL\\ DKFGGEHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQN\\ PTDVARSNPKSPQKPIVRVFLPNKQRTVVSQF$

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 ${\tt MHSNKENNSYWNLWGTELIFLFLALHQWIPLHLLPLLAFQCYLHLFQFFKIPQMWHGATPSHHKNLSLESSCPTN} \\ {\tt RGQW}$

FIGURE 2F

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 $\verb|LVSKQRILVYMLVLLQKHPSRQGDMENLQPSSSHHHGSICSYFLSLVFVQFVNIKTQFCSSNLFLKIQNFQCIS|$

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```
1 atggcggcgc tgagcggtgg cggtggtggc ggcgcggagc cgggccaggc tctgttcaac
  61 ggggacatgg agcccgaggc cggcccggc cggcccgcgg cctcttcggc tgcggaccct
 121 gccattccgg aggaggtgtg gaatatcaaa caaatgatta agttgacaca ggaacatata
 181 gaggccctat tggacaaatt tggtggggag cataatccac catcaatata tctggaggcc
 241 tatgaagaat acaccagcaa gctagatgca ctccaacaaa gagaacaaca gttattqqaa
 301 tctctgggga acggaactga tttttctgtt tctagctctg catcaatgga taccgttaca
 361 tettetteet ettetageet tteagtgeta cetteatete ttteagtttt teaaaateee
 421 acagatgtgg cacggagcaa ccccaagtca ccacaaaaac ctatcgttag agtcttcctg
 481 cccaacaaac agaggacagt ggtacctgca aggtgtggag ttacagtccg agacagtcta
 541 aagaaagcac tgatgatgag aggtctaatc ccagagtgct gtgctgttta cagaattcag
 601 gatggagaga agaaaccaat tggttgggac actgatattt cctggcttac tggagaagaa
 661 ttgcatgtgg aagtgttgga gaatgttcca cttacaacac acaactttgt acgaaaaacg
 721 tttttcacct tagcattttg tgacttttgt cgaaagctgc ttttccaggg tttccgctgt
 781 caaacatgtg gttataaatt tcaccagcgt tgtagtacag aagttccact gatgtgtgtt
 841 aattatgacc aacttgattt gctgtttgtc tccaagttct ttgaacacca cccaatacca
 901 caggaagagg cgtccttagc agagactgcc ctaacatctg gatcatcccc ttccgcaccc
 961 gcctcggact ctattgggcc ccaaattctc accagtccgt ctccttcaaa atccattcca
1021 attccacage cetteegace ageagatgaa gateategaa ateaatttgg geaacgagae
1081 cgatcctcat cagctcccaa tgtgcatata aacacaatag aacctgtcaa tattgatgac
1141 ttgattagag accaaggatt tcgtggtgat ggaggatcaa ccacaggttt gtctgctacc
1201 ccccctgcct cattacctgg ctcactaact aacgtgaaag ccttacagaa atctccagga
1261 cctcagcgag aaaggaagtc atcttcatcc tcagaagaca ggaatcgaat gaaaacactt
1321 ggtagacggg actcgagtga tgattgggag attcctgatg ggcagattac agtgggacaa
1381 agaattggat ctggatcatt tggaacagtc tacaagggaa agtggcatgg tgatgtggca
1441 gtgaaaatgt tgaatgtgac agcacctaca cctcagcagt tacaagcctt caaaaatgaa
1501 gtaggagtac tcaggaaaac acgacatgtg aatateetac tetteatggg etatteeaca
1561 aagccacaac tggctattgt tacccagtgg tgtgagggct ccagcttgta tcaccatctc
1621 catatcattg agaccaaatt tgagatgatc aaacttatag atattgcacg acagactgca
1681 cagggcatgg attacttaca cgccaagtca atcatccaca gagacctcaa gagtaataat
1741 atatttcttc atgaagacct cacagtaaaa ataggtgatt ttggtctagc tacagtgaaa
1801 tctcgatgga gtgggtccca tcagtttgaa cagttgtctg gatccatttt gtggatggca
1861 ccagaagtca tcagaatgca agataaaaat ccatacagct ttcagtcaga tgtatatgca
1921 tttgggattg ttctgtatga attgatgact ggacagttac cttattcaaa catcaacaac
1981 agggaccaga taatttttat ggtgggacga ggatacctgt ctccagatct cagtaaggta
2101 gatgagagac cactetttee ccaaattete geetetattg agetgetgge eegeteattg
2161 ccaaaaattc accgcagtgc atcagaaccc tccttgaatc gggctggttt ccaaacagag
2221 gattttagtc tatatgcttg tgcttctcca aaaacaccca tccaggcagg gggatatggt
2281 gcgtttcctg tccactga
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MAALSGGGGGGAEPGQALFNGDMEPEAGAGRPAASSAADPAIPEEVWNIKQMIKLTQEHIEALLDKFGGEHNPPS
IYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQNPTDVARSNPKS
PQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPIGWDTDISWLTGEELHVEV
LENVPLTTHNFVRKTFFTLAFCDFCRKLLFQGFRCQTCGYKFHQRCSTEVPLMCVNYDQLDLLFVSKFFEHHPIP
QEEASLAETALTSGSSPSAPASDSIGPQILTSPSPSKSIPIPQPFRPADEDHRNQFGQRDRSSSAPNVHINTIEP
VNIDDLIRDQGFRGDGGSTTGLSATPPASLPGSLTNVKALQKSPGPQRERKSSSSSEDRNRMKTLGRRDSSDDWE
IPDGQITVGQRIGSGSFGTVYKGKWHGDVAVKMLNVTAPTPQQLQAFKNEVGVLRKTRHVNILLFMGYSTKPQLA
IVTQWCEGSSLYHHLHIIETKFEMIKLIDIARQTAQGMDYLHAKSIIHRDLKSNNIFLHEDLTVKIGDFGLATVK
SRWSGSHQFEQLSGSILWMAPEVIRMQDKNPYSFQSDVYAFGIVLYELMTGQLPYSNINNRDQIIFMVGRGYLSP
DLSKVRSNCPKAMKRLMAECLKKKRDERPLFPQILASIELLARSLPKIHRSASEPSLNRAGFQTEDFSLYACASP
KTPIQAGGYGAFPVH

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1 atggagcaca tacagggagc ttggaagacg atcagcaatg gtttcggact caaagatgct 61 gtgtttgatg gctccagttg catctcccct acaattgttc agcagtttgg ctatcagcgt 121 cgggcctctg atgatggcaa actcacggat tcttctaaga caagcaatac tatccqqqtt 181 ttcttgccga ataagcaaag gactgtggtc aatgtgcgga atgggatgag cttgcacgac 241 tgccttatga aagctctgaa ggttagaggc ctgcagccag agtgctgtgc agtgttcaga 301 cttcttcagg agcacaaagg taagaaagca cgcttagatt ggaacaccga cgccgcctct 361 ctgattggag aagaactgca agtggatttt ttggatcacg ttccactcac aactcacaac 421 tttgctcgga aaacgttcct gaagcttgca ttctgtgaca tctgtcaaaa gttcctgcta 481 aatggatttc gatgtcagac ttgtggctac aagtttcatg agcactgtag caccaaagta 541 cctactatgt gtgtggactg gagtaatatc agacagctct tgctgtttcc aaattccact 601 gcaagtgaca gtggagtccc agcaccaccc tctttcacaa tgcgtcggat gcgagaatct 661 gtttcccgga tgcctgctag ttcccagcac agatactcca caccccatgc cttcactttc 721 aacaceteca geeetteete tgaaggttee etgteecaga ggeagaggte aacgteeact 781 cccaatgtcc acatggtcag caccacctg cctgtggaca gcaggatgat tgaggatgca 841 attegaagte acagtgaate agecteacet teagecetgt ecageageee caacaacetg 901 agcccaacag gctggtcaca gcccaaaacc cctgtgccag cacaaagaga gagggcgcca 961 ggatctggga cccaggaaaa aaacaaaatt aggcctcgtg ggcagagaga ttcaagttat 1021 tactgggaaa tagaagccag tgaggtgatg ctgtctactc qqattqqctc qqqctccttt 1081 ggcactgtgt acaagggcaa gtggcatgga qatqttgcag taaagatcct aaaggtggtt 1141 gacccaactc cagagcaact tcaggccttc aggaacgagg tggctgtttt gcgcaaaaca 1201 cggcatgtta atatcctgct gttcatgggg tacatgacaa aggacaacct ggcgattgtg 1261 acccagtggt gtgaaggcag cagtctctac aaacacctgc atgtccagga gaccaaattc 1321 cagatgttcc agctaattga cattgcccgg cagacagctc agggaatgga ctatttacat 1381 gcaaagaaca tcatccacag agacatgaaa tccaacaata tatttctcca tgaaggcctc 1441 acggtgaaaa tcggagattt tggtttggca acagtgaagt cgcgctggag tggttctcag 1501 caggttgaac agcccactgg ctctgtgctg tggatggccc cagaagtaat ccgaatgcag 1561 gataacaacc cgttcagctt ccagtccgat gtctactcct atggcattgt gctgtatgag 1621 ctgatgactg gggagcttcc ctactcccac atcaacaacc qaqaccaqat catcttcatq 1681 gtgggccgtg ggtacgcctc cccagatctt agcaggctct acaagaactg ccccaaggca 1741 atgaagaggt tggtggctga ctgtgtgaag aaagtcaaag aagaaaggcc tttgtttcct 1801 cagatectgt ettecattga getgetteag eactetetge egaaaateaa eaggagegee 1861 totgageett coetgeateg ggeageteae actgaggaea teaatgettg tacgetgaee 1921 acatececaa ggetaceagt ettetag

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MEHIQGAWKTISNGFGLKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTDSSKTSNTIRVFLPNKQRTVVNVRNG MSLHDCLMKALKVRGLQPECCAVFRLLQEHKGKKARLDWNTDAASLIGEELQVDFLDHVPLTTHNFARKTFLKLA FCDICQKFLLNGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNSTASDSGVPAPPSFTMRRMRESVSRMP ASSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVHMVSTTLPVDSRMIEDAIRSHSESASPSALSSSPNNL SPTGWSQPKTPVPAQRERAPGSGTQEKNKIRPRGQRDSSYYWEIEASEVMLSTRIGSGSFGTVYKGKWHGDVAVK ILKVVDPTPEQLQAFRNEVAVLRKTRHVNILLFMGYMTKDNLAIVTQWCEGSSLYKHLHVQETKFQMFQLIDIAR QTAQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLATVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDNNPF SFQSDVYSYGIVLYELMTGELPYSHINNRDQIIFMVGRGYASPDLSRLYKNCPKAMKRLVADCVKKVKEERPLFP QILSSIELLQHSLPKINRSASEPSLHRAAHTEDINACTLTTSPRLPVF

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1 atggagggtg gctgtggaga aggcggcggc ggcacgggct ccggccggag cgccgcagcg
 61 gcgcgccgag cggggagaat gaggccgaga gcgcagggcc cggactcgga gagcggcggc
 121 gaggegtece ggeteaacet gttggacaet tgegeegtgt geeaceagaa cateeagage
 181 eggqtqccca agctqctqcc ctgcctgcac tcgttctgcc agcgctgttt gcccgcgccg
 241 cagcgctate teatgetgae ggegeeegeg etgggetegg cagagaeece tecacceget
 301 cocqccccq cocccqcccc gggctccccq gccggtggtc cttcgccatt cgccacccaa
 361 gttggagtca ttcgatgccc agtttgcagt caagagtgtg ctgagagaca catcatagac
 421 aacttttttg tqaaqqacac cactqaaqtt cctaqtaqta cagtagaaaa gtctaatcag
 481 gtatqtacaa gctgtqaaqa caatgcagaa gctaatgggt tttgtgtaga gtgtgttgaa
 541 tggctctgca agacatgtat tagagctcac cagagggtga agttcacaaa agaccacaca
 601 gtcaggcaga aagaagaagt atctccagag gcagttgggg tgaccagtca gcgaccagtg
 661 ttttgtccct tccataaaaa ggagcagttg aaactttact gtgaaacatg tgataaactg
 721 acctgtcgag actgccagct gctagaacac aaagaacaca ggtatcaatt tatagaagaa
 781 gcttttcaga atcaaaaagt gatcatagat actctaatca ccaaactgat ggaaaaaaca
 841 aaatatataa agtatacagg aaatcagatc caaaatagga taattgaaat aaatcaaaac
 901 caaaagcagg tggaacagga tattaaagtt gccatcttca cattgatggt ggagataaac
 961 aaaaaaggga aagctctgct gcaccagctt gagaaaacac ttggtagaag agattcaagt
1021 gatgactggg agattcctga tggacagatt acagtgggac agagaattgg atctgggtca
1081 tttqqaactq tctacaaqqq aaaqtqqcat qqtqatqtqq cagtqaaaat gttgaatgtq
1141 acagcaccca cacctcaaca gctacaggcc ttcaaaaatg aagtaggagt gctcaggaaa
1201 actogacaty tgaatatoot cottttoaty ggotattota caaagooaca actggcaatt
1261 gttacacagt ggtgtgaggg ctccagctta tatcaccatc tccacatcat tgagaccaaa
1321 tttqaqatqa tcaaacttat aqatattqct cqqcaqactq cacaqggcat ggattactta
1381 cacqccaaqt caatcatcca caqaqacctc aaqaqtaata atatatttct tcatgaagac
1441 ctcacggtaa aaataggtga ctttggtcta gccacagtga aatctcggtg gagtgggtcc
1501 catcagtttg aacagttgtc tggatctatt ttgtggatgg caccagaagt aatcagaatg
1561 caagataaaa acccgtatag ctttcagtca gatgtgtatg cgtttgggat tgttctgtac
1621 qaactgatga ccggccagct accttattca aacatcaaca acagggatca gataattttt
1681 atggtgggac gaggatacct atctccagat ctcagtaagg tacggagtaa ctgtccaaaa
1741 gccatgaaga gattaatggc agagtgcctc aaaaagaaaa gagacgagag accactcttt
1801 ccccaaattc tcgcctccat tgagctgctg gcccgctcat tgccaaaaat tcaccgcagt
1861 qcatcaqaac cttccttqaa tcqqqctqqt ttccaaacaq aagattttag tctqtatqct
1921 tgtgcttctc cgaaaacacc catccaagca gggggatatg gtgggtttcc agtccactga
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MEGGCGEGGGTGSGRSAAAARRAGRMRPRAQGPDSESGGEASRLNLLDTCAVCHQNIQSRVPKLLPCLHSFCQR CLPAPQRYLMLTAPALGSAETPPPAPAPAPAPAPGSPAGGPSPFATQVGVIRCPVCSQECAERHIIDNFFVKDTTEV PSSTVEKSNQVCTSCEDNAEANGFCVECVEWLCKTCIRAHQRVKFTKDHTVRQKEEVSPEAVGVTSQRPVFGPFH KKEQLKLYCETCDKLTCRDCQLLEHKEHRYQFIEEAFQNQKVIIDTLITKLMEKTKYIKYTGNQIQNRIIEINQN QKQVEQDIKVAIFTLMVEINKKGKALLHQLEKTLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKWHGDVAV KMLNVTAPTPQQLQAFKNEVGVLRKTRHVNILLFMGYSTKPQLAIVTQWCEGSSLYHHLHIIETKFEMIKLIDIA RQTAQGMDYLHAKSIIHRDLKSNNIFLHEDLTVKIGDFGLATVKSRWSGSHQFEQLSGSILWMAPEVIRMQDKNP YSFQSDVYAFGIVLYELMTGQLPYSNINNRDQIIFMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKKRDERPLF PQILASIELLARSLPKIHRSASEPSLNRAGFQTEDFSLYACASPKTPIQAGGYGGFPVH

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	10 	20 	30 	40 I	50 I	60 I	70 	08		
Human Rat	ATGGCGGCGCTGA									
Mouse	ACATACAGGAGCT-TGG									
Prim.cons.	$\tt ATGGCGGCGCTGAGCGGTGGCGGCGGCATGGAGCCGGGCCAGGCTCTGTTCAAC22GGACAGGGAGCTGTGGAGGGGGGGGGG$									
	90	100	110 	120 	130 	140 	150	160		
Human	ccecceccecce		TCTTCGGCTG	CGGACCCTGC	CATTCCGGAGG	AGGTGTGGA				
Rat Mouse	AAGGCG	ATCAGCAA G-CGGCGGCA	TGGTTT CGGGCT	CGGAC CCGGC			TCAAA CGGA			
Prim.cons.	* ** * ** * * * * * * * * * * * * * *									
	170	180	190	200	210	220	230	240		
Human	 AAGTTGACACAGG	 AACATATAGA	ا GGCCCTATTG	 GACAAATTTG	 GTGGGGAGCAT	l 'AATCCACCA'	 CAATATATCT	GGAGGC		
Rat Mouse	G	ATG	CTGT	GTTTG		CT-CCA	STTGCATCTCC	C		
Prim.cons.	AAGTTGACACAGG.		*		**	* * *		*		
	250	260	270	280	290	300	310	320		
	1	1	1	1	1	1	ŀ	Ī		
Human Rat	CTATGAAGAATAC CTACAATTG									
Mouse	CGAGAGCGCAGGG	CCCGGACT	CGGAGAG		CGGCGG	CGAGGCGT	CCCG	GCTC		
Prim.cons.	CTA3222GAAT3G	3CCAGCAA3T	TGGATA3ACT	CCAACAAAGA	GAACAGCGGTT	'ATTGGGGCC1	CTG22GAACG	GCACTG		
	330	340 	350 	360 I	370	380	390	400		
Human	ATTTTTCTGTTTC	PAGCTCTGCA	TCAATGGATA	CCGTTACATC						
Rat Mouse		-AACTC -AACCT	ACGGAT- GTTGGACA		CTT	'CTAA 'GCGCC	·			
Prim.cons.	ATTTTTCTGTTTC	* *	***		***					
	410	420	430	440	450	460	470	480		
Human	CTTTCAGTTTTTC									
Rat Mouse										
Prim.cons.	CTTTCAGTTTTTC	AAAATCCCAC	* ** AG2TGTG3CA	** CGGAGCAACC	CCAAGTCACCA	* CAAAAACCTA	* \3CATCCGGGT	* CTTC3T		
	490 1	500	510 	520	530	540	550	560		
Human	GCCCAACAAACAG		GGTACCTGCA							
Rat Mouse	GCCGAATAAGCAA GCCCAAGCTGCTGG							CATGCT * * *		
Prim.cons.	GCCCAA3AAGCAG	AGCTGACTGT	GGTC33TGTG	CGGAGTGG3G	TTAGC3TGCGC	GACAGCCTTA	TGAAAGC2CT	GATG3T		
	570 I	580 I	590 I	600 I	610 	620 I	630 I	640 I		
Human Rat	GAGAGGTCTAATC									
Mouse	TAGAGGCCTGCAGG				CACCCGCTCCC	GCCCCGCCC	ccgc-cccg	GCTCCC		
Prim.cons.	GAGAGG2CTGC3C	CCAGAGTGCT	* ** GTGCTGTGTA	CAGACTTCT2	* CA22AGCAC33	* AG33AAGAAA	* * CCACGC2T3G			
	650	660	670	680	690	700	710	720		
Human	ACACTGATATTTC	I CTGGCTTACT	I GGAGAAGAAT'	 IGCATGT-GG	। AAGTGTTGGAG	I AATGTTCCAC	I TTACAACACA	 CAACTT		
Rat Mouse	ACACCGACGCCGCCCCCCCCCCCCCCCCCCCCCCCCCC			CCCAAGTTGG	AGTCATTCGA-		TTGCAG-TCA	AGAGTG		
Prim.cons.	* * * * ACACCGATG3T3C	TCGCT2ATT	GGAGAAGAA2	** ** ** rgcaagttgg.		ZATGTTCCAC	* ** ** TTACAACTCA	* * CAACTT		
	730	740 I	750 I	760	770	780 I	790	800		
Human	TGTACGAAAAACG	•		rgacttttgt	CGAAAGCTG	•	GTTTCCGCTG	TCAAA-		

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Rat Mouse	TGCTCGGAAAACG TGCT-GAGAGACA							
Prim.cons.	TGCTCGAAAAACGTTTCT3A33CTAGCATTTTGTGAC3T3TGTCACTAAAGTTCCT33TA3A3GG3TT3CGATGTCAAAT							
	810 I	820 	830 I	840	850	860	870	880
Human Rat Mouse	CATGTGGTTATAA CTTGTGGCTACAA CAGGTATGTACAA	ATTTCACCAG	CGTTGTAGT <i>A</i> CACTGTAGC <i>A</i>	CCAAAGTAC	CTACT-ATGTG	TGTGGACTG-	GAGTAATATC	AGACAGC
Prim.cons.	CATGTGG3TACAA	GTTTCATGAG	CACTGTAGTA	CAGAAGT2C	TACT2ATGTG	TGTTGA3TAT	GAGTAAT2TT	GAAT3GC
	890	900	910	920	930	940	950	960
Human Rat	TGTTTG		CTTTGAACAC		CACAGGAAGA CCACTGCAA			
Mouse	TCTGCAAGACATG	TATTAGAGCT			CACCAGAG	G	GTGAAGT~~~?	rcacaaa * *
Prim.cons.	TCTT22AGACATG	T3TCCAAGTT	CTTTGAACAC	CACCCAATAC	CAC3GGAAGA	GG2G2CCTTA	GTGGAG2CTG'	CCCAAC
	970 I	980 I	990 I	1000 !	1010	1020	1030	1040
Human Rat	ATCTGGATCATCC				ACTCTAT			
Mouse	AGACCACAC					TGGGGTGACC		
Prim.cons.	ATCTGGACCACCC		AAAGAAGAAG	T2GC3TCGG	. * A3GC3AGAATT		AGAT3CC3AC	CAGT22T
	1050	1060 	1070 	1080	1090	1100	1110	1120
Human	CCGTCTCC	TTCAAAAT	CCAT					
Rat Mouse	CCAGCACAGATAC TTGTCCCT							
Prim.cons.	* * CCGTC3CAGATAC	* ** * TCCA3AA3AA	* * GAGCCAT22	AAACTTCACT	* * * TTCA2ACACC	* * T3ACAGACC33	* * ** 3CCT3TGAAG <i>I</i>	* ATT3CC3
	1130	1140	1150	1160	1170	1180	1190	1200
Human	 A-AATCAATTTGG	GCAACGAGAC	 	1 CACCTCCCA7	 TCT		1	1
Rat Mouse	G-TCCCAGAG GCTGCTAGAAC	GCAGAGGT	CAACGT	CCACTCCCAA		CCACATGG	rcage-acca	CCTGCC
Prim.cons.	* GCT3CCAG2TTAG	** ** ;	* * CAATCC2CAT	* * * CAACTCCCAA	* * AAGAAGCTGT	** * 3CA3AATTA22	* * * 22agcgaccar	* PAGA 3CC
	1210	1220	1230	1240	1250	1260	1270	1280
	1	ı	1	1	1	i	I	1
Human Rat Mouse	TGTCAATATTGAT TGTGGACAGC-AG TCTAATCACC	GATGATTG	AGGATGC	A-ATTCGAAG	T-CACAGTGA	ATCAGCCTCAC	CCTTCAC	CC-CTG
Prim.cons.	TGT3AACA3CGA2	GA22TGATTG	AAGA322AG3	ATATTCGAAG	TA3ACAG3GA	ATCAGCC3CA3	* B3TTAGGATA3	BCTGCTA
	1290	1300	1310	1320	1330	1340	1350	1360
Human Rat	CCCCCCCTGCCTC TCCAGCAGCCCCA				GCCTTACAGA GCCCA		I GGACCTCA GTGCCAGO	I A-GCGAG C-ACAAA
Mouse	TAAATCAAAACCA		rggaacagga		GTTGC			
Prim.cons.	TCCA3CA33CCCA	A2AACCTGAGO	3CAACAGGC			AATCTCCACAT	rTGGTGCC3GA	GACAAA
	1370 	1380	1390 	1400	1410	1420	1430	1440
Human Rat Mouse	AAAGGAAGTCATC GAGAGAGGGCGCC CAAAAAAGGGA	TTCATCCTCAG AGGATCTGG	SAAGACAGGA GACCCAGGA GC-TGCACCA	AAAAAACAAA	ATTAGGCCTC AACACTTG	GTGGGCAGAGA GTAGAAGA	-GACTCGAGTG AGATTCAAGTT	ATTACT ATGACT
Prim.cons.	3AAAGAAGGCA2C							
	1450	1460 	1470	1480	1490	1500	1510	1520
Human Rat Mouse	GGGAGATTCCTGA GGGAAATAGAAGC GGGAGATTCCTGA	TGGGCAGATTA CAGTGAGGTGA	TGCTGTCTA	CTCGGATTGG	CTCGGGCTCC'	PTTGGCACTGT	GTACAAGGGC	AAGTGG
	**** ** *	* ** * *	**	* ****	** ** **	**** ** **	*****	*****
Prim.cons.	GGGAGATTCCTGA	LGGJCAGATTA	CAGTGGGAC	AJAGAATTGG	ATCTGG3TCA	TTGGAACTGT	CTACAAGGGA	AAGTGG

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Human Rat Mouse	1530 CATGGTGATGTGG CATGGAGATGTTGG CATGGTGATGTGGG	AGTAAAGAT	CCTAAAGGTG	GTTGACCCAA	CTCCAGAGCA	ACTTCAGGCCT	TTCAGGAACG	AGGTGGC
Prim.cons.	CATGGTGATGTGG	AGTGAAAAT	GTTGAATGTG.	ACAGCACC3A	CACCTCAGCA		TCAAAAATG	
	1610	1620	1630	1640	1650	1660	1670	1680
Human Rat M ouse	AGTACTCAGGAAAA TGTTTTGCGCAAAA AGTGCTCAGGAAAA	CACGGCATG	TAATATCCT	GCTGTTCATG	GGTACATGA	CAAAGG-ACAA	CCTGGCGAT	TGTGACC
Prim.cons.	AGT3CTCAGGAAAA	CACGACATG	* ******** IGAATATCCT:	** ****** 3CT3TTCATG	GGCTATTC3A	CAAAGCCACAA	CCTGGC3AT	*** ** FGTTACC
	1690	1700	1710	1720	1730	1740	1750	1760
Human Rat Mouse	CAGTGGTGTGAGGG CAGTGGTGTGAAGG CAGTGGTGTGAGGG	CAGCAGTCT	CTACAAACAC	CTGCATGTCC	AGGAGACCAA	ATTCCAGATGT	TCCAGCTAAT	TTGACAT
Prim.cons.	CAGTGGTGTGAGGG	CTCCAGCTT	STATCACCAT	CTCCATATCA:	TTGAGACCAA	ATTTGAGATGA	TCAAACTTA	ragatat
	1770 	1780 	1790 I	1800 I	1810	1820	1830	1840
Human Rat Mouse	TGCACGACAGACTG TGCCCGGCAGACAG TGCTCGGCAGACTG	CTCAGGGAA	rggactattt?	ACATGCAAAG	ACATCATCC	CAGAGACATG	AAATCCAACA	TATATA
Prim.cons.	TGC3CGGCAGACTG	CACAGGGCA	rggattactti	ACACGCCAAG	CAATCATCC	ACAGAGACCTC	AAGAGTAAT <i>I</i>	TATATA
	1850 I	1860	1870	1880	1890	1900	1910	1920
Human Rat Mouse	TTCTTCATGAAGAC TTCTCCATGAAGGC TTCTTCATGAAGAC	CTCACGGTG <i>I</i> CTCACGGTA <i>I</i>	AAATCGGAGA	ATTTTGGTTT(ACTTTGGTCT <i>I</i>	GCAACAGTGA	AGTCGCGCTG	GAGTGGTTCT	CAGCAG
Prim.cons.	TTCTTCATGAAGAC	CTCACGGTA	\AAATAGGTG!	ATTTTGGTCT?	AGC3ACAGTGA	AATCTCG3TG	GAGTGGGTCC	CCATCAG
	1930	1940	1950	1960	1970	1980	1990	2000
Human Rat Mouse	TTTGAACAGTTGTC GTTGAACAGCCCAC TTTGAACAGTTGTC	TGGCTCTGT	CTGTGGATG	CCCCAGAAG	AATCCGAATC	CAGGATAACA	ACCCGTTCAG	CTTCCA
Prim.cons.	TTTGAACAGTTGTC	TGGATCTATI	TTGTGGATG	GCACCAGAAGI	AATCAGAATG	CAAGATAAAA	ACCCGTACAG	CTTTCA
	2010 	2020 	2030 	2040 I	2050	2060 I	2070 I	2080
Human Rat Mouse	GTCAGATGTATATG GTCCGATGTCTACT GTCAGATGTGTATG	CCTATGGCAT	TGTGCTGTAT	GAGCTGATGA	CTGGGGAGCT	TCCCTACTCC	CACATCAACA	ACCGAG ACAGGG
Prim.cons.	GTCAGATGT3TATG	C3TTTGGGA1	TGTTCTGTAT	GAACTGATGA	CTGG3CAGCT	'ACCTTATTCA	AACATCAACA	ACAGGG
Human	2090 ACCAGATAATTTT							
Rat Mouse	ACCAGATCATCTTC. ATCAGATAATTTTT	ATGGTGGGAC	GAGGATACCT	ATCTCCAGAT		TACGGAGTAA	CTGTCCAAAA	GCCATG
Prim.cons.	ACCAGATAATTTTT.						*** ** ** CTGTCCAAAA	
Human Rat	2170 AAGAGATTAATGGC. AAGAGGTTGGTGGC							
Mouse	AAGAGATTAATGGC							
Prim.cons.	AAGAGATTAATGGC	AGAGTGCCTC	AAAAAGAAAA	GAGA3GAGAG	ACCACTCTTT	CCCCAAATTC	TCGCCTCCAT	TGAGCT
	2250 	2260 	2270 	2280 I	2290 1	2300 I	2310	2320
Human	GCTGGCCCGCTCAT	rgccaaaaat	TCACCGCAGT	GCATCAGAAC	•	TCGGGCTGGT	rtccaaacag	AGGATT

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2330 2340 2350 2360 2370 2380 2390

Prim.cons. TTAGTCT2TATGCTTCTCCGAAAACACCCATCCA2GCAGGGGGATATGGTG2GTTTCCAGTCCACTGA

Alignment data :

Alignment length: 2394
Identity (*): 976 is 40.77 %
Strongly similar (:): 0 is 0.00 %
Weakly similar (.): 0 is 0.00 %
Different: 1418 is 59.23 %

Sequence 0001 : Human (2298 residues). Sequence 0002 : Rat (1947 residues). Sequence 0003 : Mouse (1980 residues).

CLUSTALW options used :

dnamatrix=iub
endgaps=1
gapdist=8
gapext=0.05
gapopen=10.0
ktuple=1
maxdiv=40
outorder=aligned
pairgap=3
score=percent
topdiags=5
type=DNA
window=5

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	10	20	30	40	50	60	70	80
Human Mouse	 ATGGCGGCGCTC ATGGAGGGTGGCTC							CATGGA CGGGGA
Prim.cons.	**** ** **** ATGG2GG2TGGCTC	** **	** ** ****	* *** *	**** * **	* * ** **	* *	* ***
	90	100	110	120	130	140	150	160
Human Mouse	GCCCGAGGCCGAGA						 GTGTGGAATA GCTCAACCTG	
Prim.cons.	G222GAGGCCG222	22CG222GGC	CGCG2C222	222GC2GCGG	ACC22G2C2T	2CCGGAGGAG	G222222 T 2	T222AC
	170	180	190	200	210	220	230	240
Human Mouse	AAATGATTAAGTTO			CCTATTGGAC	AAATTTGGTG	GGGAGCATAA GGGTGCCCAA		
Prim.cons.	A22TG222222TG	32CAC22GAA	CAT22AGAGGC	CCTATTGGAC	AAATTTGGTG	GGG2GC22AA	2C22C22C2	ATAT22
	250	260	270	280	290	300	310	320
Human Mouse	CTGGAGGCCTATGA		CAGCAAGCTAG CAGCGCTGT			ACAACAGTTAT GCCGCAGCGCT * ***		
Prim.cons.	CTG2AGGC222TG	AAGAAT222C	CAGCAAGCT22	2TGC2C2CCA	ACAAAGAGA2	C22CAG222T	TGGAATCTC2	2G222A
	330 I	340 I	350 I	360 I	370 I	380 I	390 I	400 I
Human Mouse	CGGAACTGATTTT		GCTCTGCATC	AATGGATACCG			AGCCTTTCAG -GCCC	TGCTAC CCGC
Prim.cons.	CGG22CTGATTT2	222G2T2CT2	GCTC2GCATC	ATGGA2ACC2	2T2CA2C220	СТ2ССТСТТСТ	AGCC2TTCAG	TGC22C
	410	420	430 I	440	450	460	470 I	480 I
Human Mouse	CTTCATCTCTTTC	•	AATCCCACAGA C-CG	ATGTGGCACGG GTGGTCCTT		AAGTCACCACA GCCACC-CA		GTTAGA GTTGGA
Prim.cons.	C22C22C2CTTT2	2G2T222C22	AATCCC2CAG	ATGTGG22C22	2GC2A22CC	AAG2CACCACA	AAAACCTATC	GTT2GA
	490 I	500 I	510	520 I	530 I	540 I	550 I	560 I
Human Mouse	GTCTTCCTGCCC					ACAGTCCGAGA ACA-TCATAGA		GTGAAG
Prim.cons.	GTC2T2CGATGCC	CA2222CAG	222A2AGTGG	r22CTGCAAGG	TGT2GAG221	ACAGTC22AGA	CA222TTTTT	GTGAA2
	570 1	580 1	590 I	600 I	610 	620 	630 I	640 I
Human Mouse	GAAAGCACTGATG GACACCACTGAAG			STGCTGTGCTG STACAGTA		TTCAGGATGGA TCTAATCAGGT * * **		
Prim.cons.	GA2A2CACTGA2G	2TGAGAGG2C	TA2TCCCAGA(ST2C2GT2CTG	TTT22A2A2	r22A2222GG2	22G2A2AA2C	2AATTG
	650 I	660 I	670 I	680 I	690 	700 	710 	720
Human Mouse	GTTGGGACACTGA' GTGAAGACAATG-		CTTACTGGAGA GCTAATGGG			GTTGGAGAATG GTTGAATG	GCTCT-GC	
Prim.cons.	GT222GACA2TGA	ratttc2222	22TA2TGG2G	AAGAATT2221	GT2GA2TGT	GTTGGAGAATG	222CACTT2C	:AA2ACA
	730 I	740 I	750 I	760 I	770 I	780 	790 I	800 I
Human Mouse	CAACTTTGTACGA.	GAGC'	TCACCTTAGC					GCTGTC CACAGTC
Prim.cons.	CAACTTTGTA22A	2A2ACGTTT2	TCACC22AG2	ATTTTGTGA22	TT22TC2AA	AGCT2CTTTTC	CAGGGTTTCC	2C2GTC
	810 	820 I	830 I	840 	850 	860 I	870 	880 I
Human Mouse	AAACATGTGGTTA AGGCA-GAAAGAA * ** *		CAGCGTTGTAG	GT	CCACTGATG	rgtgttaatta rg-accagtca ** * *		

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Prim.cons.	A22CATG22222A2A	A2T2TC2CCA	G2GTTG2AG1	ACAGAAGTTC	CACTG22GTG	T222A2T2AG	2GACCA2CTT	GAT2T
	890	900	910 I	920 I	930	940 I	950 I	960 L
Human Mouse	GCTGTTTGTCTCCAAC		CACCACCCA	ATACCACAGGA -TTCCATAAAA		•	CTTTACTG	ATCTG TG
Prim.cons.	GCTGTTTGTC2CCAA	GTTCTTTGAA	CACCACCCA	AT2CCA2A22A	AG22GCGTCC	TTAG22GA2A	CT222CT2AC	ATCTG
	970	980 I	990	1000	1010 I	1020	1030	1040 I
Human Mouse	GATCATCCCCTTCCGC AAACATG'	CACCCGCCTC		CGAGAC	TTCTCACCAG			
Prim.cons.	2A2CATCCCCTTCCG	222222CTC	GGACTCT2T2	2G2G2CCCAA <i>F</i>	ATTCTC2CCAG	TCCGTCT2CT	TCA2AA22CA	TTCCA
	1050	1060	1070	1080	1090	1100	1110	1120
Human Mouse	ATTCCACAGCCCTTC	 CGACCAGCAG CAATTTATAG * * *	ATGAAGATCA AAGAAGCTTT	ATCGAAATCA!	ATTTGGGCAAC AAAAGTGAT * * *	GAGACCGATC	CTCATCAGCT	CCCAA -CCAA
Prim.cons.	A222CACAG2CCT22	C2A22222AG	A2GAAG2T22	2TC22AATCA	32TT22G22A2	2A2A222A22	CT2ATCAGCI	CCCAA
	1130	1140	1150 	1160 	1170 	1180 !	1190 	1200
Human Mouse	TGTGCATATAAACAC.	AATAGAACCI AACAAAATAI	GTCAATA	ATTGATGACT	rgattagagac	'AGGATAAT	CGTGGTGATG TGAAATAAAT	GAGGA CAAAA * *
Prim.cons.	22TGCATAT22A2A2	AA2A2AA22T	2T2AAGTAT	A22G222A22	2GAT222A2A2	CAAGGAT2AT	2G222T2A22	2A22A
	1210	1220	1230	1240	1250	1260	1270	1280
Human Mouse	TCAACCACAGGTTTG CCAAAAGCAGGTGGA	TCTGC-TACC	CCCCCTGCC	CATTACCTGG	CTCACTAACT CTCACATT	'GATGG	CCTTACAGAA TGGAC	ATCTC
Prim.cons.	2CAA222CAGGT222	2C2G2ATA22	22222 T GCC	TCATTA2CTG	GCTCACTAA21	2A2GTGAAAG	2CTTAC2GA2	AT2TC
	1290	1300	1310	1320 I	1330 I	1340 l	1350 	1360
Human Mouse	CAGGACCTCAGCGAG	AAAGGAAGTO AAAGGGAAAO	ATCTTCATC	CTCAGAAGAC ACCAG	AGGAATCGAAT CTTGA * **	GAAAACACTT GAAAACACTT	GGTAGACGG(SACTCG SATTCA
Prim.cons.	CAGGACCTCA2C2A2	AAAGG2A222	2TCT2C22C	22CAGAAGAC	2GGAAT2GAAT	GAAAACACTT	GGTAGA2G20	SA2TC2
	1370	1380	1390 	1400 	1410	1420 I	1430 I	1440
Human Mouse	AGTGATGATTGGGAG AGTGATGACTGGGAG	ATTCCTGAT	GGCAGATTA GGACAGATTA	CAGTGGGACA CAGTGGGACA ******	GAGAATTGGAT	CTGGGTCATT	TGGAACTGT	CTACAA
Prim.cons.	AGTGATGA2TGGGAG	ATTCCTGATO	GG2CAGATTA	CAGTGGGACA	2AGAATTGGA:	rCTGG2TCATT	TGGAAC2GT	
	1450 I	1460 	1470 	1480 	1490 	1500 	1510 1	1520 I
Human Mouse	GGGAAAGTGGCATGG GGGAAAGTGGCATGG	TGATGTGGC	AGTGAAAATG *******	TTGAATGTGA	CAGCACCCAC	ACCTCAACAGO	TACAGGCCT	CAAAA *****
Prim.cons.	GGGAAAGTGGCATGG	TGATGTGGC	AGTGAAAATG	TTGAATGTGA	CAGCACC2AC	ACCTCA2CAG2	TACA2GCCT	CAAAA
	1530 	1540 	1550 	1560 	1570 	1580 	1590 	1600
Human Mouse	ATGAAGTAGGAGTAC ATGAAGTAGGAGTGC	TCAGGAAAA TCAGGAAAA	CACGACATGT CTCGACATGT	GAATATCCTA GAATATCCTC *******	CTCTTCATGG CTTTTCATGG ** ******	GCTATTCCACA GCTATTCTACA *******	AAAGCCACAA AAAGCCACAA *******	CTGGCT CTGGCA
Prim.cons.	ATGAAGTAGGAGT20	TCAGGAAAA	C2CGACATGT	GAATATCCT2	CT2TTCATGG	GCTATTC2AC <i>I</i>	AAAGCCACAA	CTGGC2
	1610 I	1620	1630	1640	1650	1660 	1670 I	1680
Human Mouse	ATTGTTACCCAGTGG		PCCAGCTTGT					CAAACT
Prim.cons.	ATTGTTAC2CAGTG	GTGTGAGGGC'	TCCAGCTT2T	ATCACCATCT	CCA2ATCATT	GAGACCAAATT	TTGAGATGAT	CAAACT
	1690	1700	1710	1720 I	1730	1740 	1750 	1760
Human Mouse	TATAGATATTGCACO TATAGATATTGCTCO	GACAGACTGC. GGCAGACTGC.	ACAGGGCATG ACAGGGCATG	GATTACTTAC	ACGCCAAGTC ACGCCAAGTC	AATCATCCACA AATCATCCACA	AGAGACCTCA AGAGACCTCA	AGAGTA

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Prim.cons. TATAGATATTGC2CG2CAGACTGCACAGGGCATGGATTACTTACACGCCAAGTCAATCATCCACAGAGACCTCAAGAGTA 1770 1800 1780 1790 1810 1820 1830 1840 ATAATATATTTCTTCATGAAGACCTCACAGTAAAAATAGGTGATTTTGGTCTAGCTACAGTGAAATCTCGATGGAGTGGG Human ATAATATATTTCTTCATGAAGACCTCACGGTAAAAATAGGTGACTTTGGTCTAGCCACAGTGAAATCTCGGTGGAGTGGG Mouse Prim.cons. ATAATATTTCTTCATGAAGACCTCAC2GTAAAAATAGGTGA2TTTGGTCTAGC2ACAGTGAAATCTCG2TGGAGTGGG 1850 1860 1870 1880 1890 1900 1910 1920 Human TCCCATCAGTTTGAACAGTTGTCTGGATCCATTTTGTGGATGGCACCAGAAGTCATCAGAATGCAAGATAAAAATCCATA Mouse TCCCATCAGTTTGAACAGTTGTCTGGATCTATTTTGTGGATGGCACCAGAAGTAATCAGAATGCAAGATAAAAACCCGTA Prim.cons. TCCCATCAGTTTGAACAGTTGTCTGGATC2ATTTTGTGGATGGCACCAGAAGT2ATCAGAATGCAAGATAAAAA2CC2TA 1930 1960 2000 CAGCTTTCAGTCAGATGTATATGCATTTGGGATTGTTCTGTATGAATTGATGACTGGACAGTTACCTTATTCAAACATCA Human Mouse TAGCTTTCAGTCAGATGTGTATGCGTTTGGGATTGTTCTGTACGAACTGATGACCGGCCAGCTACCTTATTCAAACATCA Prim.cons. 2AGCTTTCAGTCAGATGT2TATGC2TTTGGGATTGTTCTGTA2GAA2TGATGAC2GG2CAG2TACCTTATTCAAACATCA 2010 2020 2030 2040 2050 2060 2070 2080 ACAACAGGGACCAGATAATTTTTATGGTGGGACGAGGATACCTGTCTCCAGATCTCAGTAAGGTACGGAGTAACTGTCCA Human Mouse Prim.cons. ACAACAGGGA2CAGATAATTTTTATGGTGGGACGAGGATACCT2TCTCCAGATCTCAGTAAGGTACGGAGTAACTGTCCA 2090 2100 2110 2120 2130 2140 2150 2160 AAAGCCATGAAGAGATTAATGGCAGAGTGCCTCAAAAAGAAAAGAGATGAGAGACCACTCTTTCCCCAAATTCTCGCCTC Human Mouse ${\tt AAAGCCATGAAGAGATTAATGGCAGAGTGCCTCAAAAAGAAAAGAAAAGAACACTCTTTCCCCAAATTCTCGCCTC}$ Prim.cons. 2170 2180 2220 2190 2200 2210 2230 2240 ${\tt TATTGAGCTGCCCGCTCATTGCCAAAAATTCACCGCAGTGCATCAGAACCCTCCTTGAATCGGGCTGGTTTCCAAA}$ Human Mouse Prim.cons. 2250 2260 2270 2280 2290 2300 2310 2320 Human Mouse CAGAAGATTTTAGTCTGTATGCTTGTGCTTCTCCGAAAACACCCATCCAAGCAGGGGGATATGGTGGGTTTCCAGTCCAC Prim.cons. CAGA2GATTTTAGTCT2TATGCTTGTGCTTCTCC2AAAACACCCATCCA2GCAGGGGGATATGGTG2GTTTCC2GTCCAC Human TGA Mouse TGA Prim. cons. TGA Alignment data : Alignment length: 2323 Identity (*) : 1505 is 64.79 % Strongly similar (:) : 0 is 0.00 % Weakly similar (.) : 0 is 0.00 % Different : 818 is 35.21 % Sequence 0001 : Human (2298 residues). Sequence 0002 : Mouse (1980 residues). CLUSTALW options used : dnamatrix=iub endgaps=1 gapdist=8 gapext=0.05 gapopen=10.0

ktuple=1

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maxdiv=40 outorder=aligned pairgap=3 score=percent topdiags=5 type=DNA window=5

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	10 	20 	30 	40 !	50 I	60 I	70 I	80 I	
Human Rat	ATGGCGGCGCTGA	AGCGGTGGCGG		GCGGAGCCGG ATGGA	GCCAGGCTCT		SACATGGAGCO -ACAGGGAGCT		
Prim.cons.	ATGGCGGCGCTG	AGCGGTGGCGG	тестессес		** GCCAGGCTCT	** GTTCAAC22G	SACA2GGAGC2	* 2G222C	
	90 I	100 	110 	120	130 	140	150	160	
Human Rat	CGGCGCCGGCCGG	SCCCGCGGCCT ATCAGCAA	TGGTTTC	GGAC	CATTCCGGAGG	AGGTGTGGAAT	PATCAAACAAA TCAAA	TGATTA	
Prim.cons.	cgcccccg2cg2	* ** 22C2GC22CCT	** * * CTT2GG2T2C		ATTCCGGAGG!	AGGTGTGGAAT	***** PATCAAACAAA	TGATTA	
	170	180	190	200	210 	220	230	240	
Human Rat	AGTTGACACAGGA		GCCCTATTGG						
Prim.cons.	* AGTTGACACAGG	** ACAT2TAGAG	** * GCCCT2TTGG	**** ACAA2TTTG2	*** TGGGGAGCAT	* *** ATC2ACCA22	** ** 222AT2TC2G	* * GAGGCC	
	250	260	270	280	290	300	310	320	
Human Rat	 TATGAAGAATACA TACAATTGI			I CAACAAAGAG	 AACAACAGTT CAGCG				
Prim.cons.	** *** TA2GAAGAAT222	***** * 2CAGCA222T	* * 2G2T22ACTC	CAACAAAGAG	** * GAACA2C2GTT#	* * * *** ATT2G222CTC	** ** ** TG22GAA2GG	* 2ACTGA	
	330	340	350	360	370	380	390	400	
Human	TTTTTCTGTTTC1	AGCTCTGCAT		I CGTTACATCT			 GTGCTACCTT	CATCTC	
Rat Prim.cons.	**************************************	* ***	ACGGAT		****	**			
FIIM. CONS.	TTTTTCTGTTTCT	420	430	440					
Human	t	1	1	1	450 	460 	470 	480 I	
Rat	TTTCAGTTTTTCAAAATCCCACAGATGTGGCACGGAGCAACCCCCAAGTCACCACAAAAACCTATCGTTAGAGTCTTCCTGTACTATCCGGGTTTTCTTG * * * * * * * * * * * * * * * * * * *								
Prim.cons.	TTTCAGTTTTTCA	AAATCCCACA	GATGTG2CAC	GGAGCAACCC	CAAGTCACCAC	AAAAACCTA2	22T22G2GT2	TTC2TG	
	490 	500 	510 	520 	530 1	540 I	550 I	560 I	
Human Rat	CCCAACAAACAGA CCGAATAAGCAAA ** ** ** ** *								
Prim.cons.	CC2AA2AA2CA2A	GGAC2GTGGT	222TG222GG2	22TGG22T2A	222T2C22GAC	2G2CT2A2GA	AAGC2CTGA2	G2T2AG	
	570 	580 	590 I	600 I	610 I	620 	630 I	640 1	
Human Rat	AGGTCTAATCCCA AGGCCTGCAGCCA				-AGGATGGAGA GAGCACAAAGG				
Prim.cons.	AGG2CT2222CCA	GAGTGCTGTG	C2GT2T2CAG	A2TTCTTCAG	GAG2A222AG2	2AAGAAA2CA	2GCTT2G2TT	GG2ACA	
	650 I	660 I	670 I	680 I	690 I	700 I	710	720 I	
Human Rat	CTGATATTTCCTG CCGACGCCGCCTC	GCTTACTGGAG TCTGATTGGAG	GAAGAATTGCA GAAGAACTGCA	AAGTGGATTT	TTTGGATCACG	TTCCACTCAC	AACACACAAC!	TTTGCT	
Prim.cons.	C2GA22222CCT2	2CT2A2TGGA	gaagaa2tgc <i>i</i>	A2GTGGA22T					
	730 1	740 I	750 {	760 I	770 I	780 I	790 I	800	
Human Rat	CGAAAAACGTTTT CGGAAAACGTTCC	TCACCTTAGC	ATTTTGTGACT ATTCTGTGAC	TTTGTCGAA.	AGCTGCTTTTC AGTTCCTGCTA	CAGGGTTTCC			
Prim.cons.	CG2AAAACGTT22					2A2GG2TT2C	G2TGTCA2AC2	2TGTGG	
	810 I	820 	830 I	840	850 I	860 I	870 I	880	
Human Rat	TTATAAATTTCAC	CAGCGTTGTAC GAGCACTGTAC	GTACAGAAGTI GCACCAAAGTA	CCTACT-ATO	GTGTGTTAATT GTGTGTGGACT	ATGACCAAC-	TTGATTTGCT(GTTT CTTGCT	

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Prim.cons.	2TA2AA2TTTCA22AGC22TGTAG2AC22AAGT2CCTACTGATGTGTGT22A2T2TGA22AA2AT222222GCT2TTGCT
	890 900 910 920 930 940 950 960
Human Rat	GTCTCCAAGTTCTTTGAACACCACCCAATACCACAGGAAGAAGGAGGCGTCCTTAGCAGAGACTGCCCTAACATCTGGATCATC GTTTCCAAATTCCACTGCAAGTGACAGTGGAGTCCCAGCACCACC
Prim.cons.	GT2TCCAA2TTCTTTGAACACCACCCAATACCAC2G2AAGAGG2G2CCTTAG22GAGACTG2CC2A2CATCTGGA2CA2C
	970 980 990 1000 1010 1020 1030 1040
Human Rat	CCCTTCCGCACCCGCCTCGGACTCTATTGGGCCCCAAATTCTCACCAGTCCGTCTCCTTCAAAATCCAT CTCTTTCACAAT-GCGTCGGATGCGAGAATCTGTTTCCCGGATGCCTAGTTCCCAGACACAGATACTCCACACCCCAT
Prim.cons.	C2CTT2C2CA22CGC2TCGGA22C2AGAAT2TG222CCC22AT2C222C2AGTTCCC22C2CAGATACT2CA2A22CCAT
	1050 1060 1070 1080 1090 1100 1110 1120
Human Rat	TCCAATTCCACAGCCCTTCCGACCAGCAGATGAAGATCATCGAAATCAATTTGGGCAACGAGACCGATCCTCATCAG GCCTTCACTTTCA-ACACCTCCAGCCCTTCCTCTGAAGGTTCCCTGTCCCAGAGGCAGAGGTCAACGTCCA
Prim.cons.	GCCT2CA2TT2CACA22CCT2C2G2CC22C22TGAAG2T222C2222CA2TTT2GGCAACGAG22C2ATCCTC2TC22
	1130 1140 1150 1160 1170 1180 1190 1200
Human Rat	CTCCCAATGTGCATATAAACACAATAGAACCTGTCAATATTGATGACTTGATTAGAGACCCAAGGATTTCGTGGTGAT CTCCCAATGTCCACATGGTCAGCACCACCCTGCCTGTGGACAGC-AGGATGATTGAGGATGCAATTCGAAGTCAC
Prim.cons.	CTCCCAATGT2CA2AT2GTCA2CAC2A22222CCTGT22A2A22GA2GACTTGATT222GA2CAAG2A2TTCG22GT2A2
	1210 1220 1230 1240 1250 1260 1270 1280
Human Rat	GGAGGATCAACCACAGGTTTGTCTGCTACCCCCCTGCCTCATTACCTG-GCTCACTAA-CTAACGTGAAAGCCTTACAGAGAGTGAATCAGCCTCACCTTCAGCC-CTGTCCAGCAGCCCCAACAACCCTGAGCCCAACAACGCTG-GTCACAGCCC-
Prim.cons.	2G2G2ATCA2CC2CA22TT222CC2GCT22CC22CC22A22ACCTGAGC2CA22A2GCT2ACGT2A2AGCCTTACAG
	1290 1300 1310 1320 1330 1340 1350 1360
Human Rat	AAATCTCCAGGACCTCAGCGAGAAAGGAAGTCATCTTCATCCTCAGAAGACAGGAATCGAATGAAAACACTTGGTAGA AAAACCCCTGTGCCAGCACAAAGAGAGAGGGCGCCAGGATCTGGGACCCAGGAAAAAAAAATTAGGCCTCGTGGG
Prim.cons.	AAA2C2CC2G22CC2222C2A22A22GA2GCC2C22CATC2TC2G2A22CAGGAA222AAA22AAA
	1370 1380 1390 1400 1410 1420 1430 1440
Human Rat	CGGGACTCGAGTGATGATTGGGAGATTCCTGATGGGCAGATTACAGTGGGACAAAGAATTGGATCTGGATCATTTGG CAGAGAGATTCAAGTTATTACTGGGAAATAGAAGCCAGTGAGGTGATGCTCTACTCGGATTGGCTCGGGCTCCTTTGG * * * * * * * * * * * * * * * * * * *
Prim.cons.	C2GAGAGA2TC2AGT2AT2A2TGGGA2AT2222G222G22AG2T2A222TG222222G2ATTGG2TC2GG2TC2TTTGG
	1450 1460 1470 1480 1490 1500 1510 1520
Human Rat	AACAGTCTACAAGGGAAAGTGGCATGGTGATGTGGCAGTGAAAATGTTGAATGTGACAGCACCTACACCTCAGCAGTTAC CACTGTGTACAAGGGCCAAGTGGCATGGAGATGTTGCAGTAAAGATCCTAAAGGTGGTTGACCCAACTCCAGAGCAACTTC ** * * * * * * * * * * * * * * * * * *
Prim.cons.	2AC2GT2TACAAGGG2AAGTGGCATGG2GATGT2GCAGT2AA2AT22T2AA2GTG222G22CC2AC2CC22AGCA22T2C
	1530 1540 1550 1560 1570 1580 1590 1600
Human Rat	AAGCCTTCAAAAATGAAGTAGGAGTACTCAGGAAAACACGACATGTGAATATCCTACTCTTCATGGGCTATTCCACAAAG AGGCCTTCAGGAACGAGGTGGCTGTTTTGCGCAAAACACGGCATGTTAATATCCTGCTGTTCATGGGGTACATGACAAAG
Prim.cons.	A2GCCTTCA22AA2GA2GT2G22GT22T22G2AAAACACG2CATGT2AATATCCT2CT2TTCATGGG2TA2222ACAAAG
	1610 1620 1630 1640 1650 1660 1670 1680
Human Rat	CCACAAC-TGGCTATTGTTACCCAGTGGTGTGAGGGCTCCAGCTTGTATCACCATCTCCATATCATTGAGACCAAATTTG G-ACAACCTGGCGATTGTGACCCAGTGGTGTGAAGGCAGCCAGTCTCTACAAACACCTGCATGTCCAGGAGACCAAATTCC
Prim.cons.	2CACAACCTGGC2ATTGT2ACCCAGTGGTGTGA2GGC22CAG22T2TA22A2CA2CT2CAT2TC222GAGACCAAATT22
	1690 1700 1710 1720 1730 1740 1750 1760
Human Rat	AGATGATCAAACTTATAGATATTGCACGACAGACTGCACAGGGCATGGATTACTTAC

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Prim.cons AGATG2TC2A2CT2AT2GA2ATTGC2CG2CAGAC2GC2CAGGG2ATGGA2TA2TTACA2GC2AAG222ATCATCCACAGA 1770 1780 1800 1810 1820 1830 1840 Human GACCTCAAGAGTAATAATATTTCTTCATGAAGACCTCACAGTAAAAATAGGTGATTTTGGTCTAGCTACAGTGAAATC Rat GACATGAAATCCAACAATATATTTCTCCATGAAGGCCTCACGGTGAAAATCGGAGATTTTGGTTTGGCAACAGTGAAGTC Prim.cons. GAC2T2AA2222AA2AATATATTTCT2CATGAAG2CCTCAC2GT2AAAAT2GG2GATTTTGGT2T2GC2ACAGTGAA2TC 1850 1860 1870 1880 1890 1900 1910 1920 TCGATGGAGTGGGTCCCATCAGTTTGAACAGTTGTCTGGATCCATTTTGTGGATGGCACCAGAAGTCATCAGAATGCAAG Human Rat GCGCTGGAGTGGTTCTCAGCAGGTTGAACAGCCCACTGGCTCTGTGCTGTGGATGGCCCCAGAAGTAATCCGAATGCAGG Prim.cons. 2CG2TGGAGTGG2TC2CA2CAG2TTGAACAG2222CTGG2TC22T22TGTGGGTGGC2CCAGAAGT2ATC2GAATGCA2G 1930 1940 1950 1960 1970 1980 Human ATAAAAATCCATACAGCTTTCAGTCAGATGTATATGCATTTGGGATTGTTCTGTATGAATTGATGACTGGACAGTTACCT Rat ATAACAACCCGTTCAGCTTCCAGTCCGATGTCTACTCCTATGGCATTGTGTGTATGAGCTGATGACTGGGGAGCTTCCC * * *** **** ***** Prim.cons. ATAA2AA2CC2T2CAGCTT2CAGTC2GATGT2TA22C2T2TGG2ATTGT2CTGTATGA22TGATGACTGG22AG2T2CC2 2010 2020 2030 2050 2060 TATTCAAACATCAACAACAGGGACCAGATAATTTTTATGGTGGGACGAGGATACCTGTCTCCAGATCTCAGTAAGGTACG Human TACTCCCACATCAACCAGCCGAGACCAGATCATCTTCATGGTGGGCCGTGGGTACGCCTCCCCAGATCTTAGCAGGCTCTA Rat Prim.cons. TA2TC22ACATCAACAAC2G2GACCAGAT2AT2TT2ATGGTGGG2CG2GG2TAC222TC2CCAGATCT2AG2A2G2T222 2110 2120 2130 2140 2150 2160 Human GAGTAACTGTCCAAAAGCCATGAAGAGATTAATGGCAGAGTGCCTCAAAAAGAAAAGAGATGAGAGACCACTCTTTCCCC CAAGAACTGCCCCAAGGCAATGAAGAGGTTGGTGGCTGACTGTGTGAAGAAAGTCAAAGAAGAAGAAGGCCTTTGTTTCCTC 2A22AACTG2CC2AA2GC2ATGAAGAG2TT22TGGC2GA2TG22T2AA2AA22222A2AGA2GA2GA2AG2CC22T2TTTCC2C 2170 2180 2190 2200 2210 2220 2230 Human AAATTCTCGCCTCTATTGAGCTGCCCGCCTCATTGCCAAAAATTCACCGCAGTGCATCAGAACCCTCCTTGAATCGG AGATCCTGTCTTCCATTGAGCTGCTTCAGCACTCTCTGCCGAAAATCAACAGGAGCGCCTCTGAGCCTTCCCTGCATCGG Rat A2AT2CT22C2TC2ATTGAGCTGCT2222C2CTC22TGCC2AAAAT22AC2G2AG2GC2TC2GA2CC2TCC2TG2ATCGG Prim.cons. 2250 2260 2270 2280 2290 2300 2310 2320 Human Rat Prim.cons. 2330 GTTTCCTGTCCACTGA Human Rat GCTACCAGTCTTCTAG G2T2CC2GTC22CT22 Prim.cons. Alignment data : Alignment length : 2336 Identity (*) : 1291 is 55.27 % Strongly similar (:) : 0 is 0.00 % Weakly similar (.) : 0 is 0.00 % Different : 1045 is 44.73 % Sequence 0001 : Human (2298 residues). Sequence 0002: Rat (1947 residues). CLUSTALW options used : dnamatrix=iub endgaps=1 gapdist=8

FIGURE 6C

gapext=0.05
gapopen=10.0
ktuple=1

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maxdiv=40 outorder=aligned pairgap=3 score=percent topdiags=5 type=DNA window=5

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>gi|1170701|sp|P15056|KRAB_HUMAN B-Raf proto-oncogene serine/threonineprotein kinase (p94) (v-Raf murine sarcoma viral oncogene homolog B1)

>Human.

MAALSGGGGGGAEPGQALFNGDMEPEAGAGRPAASSAADPAIPEEVWNIKQMIKLTQEHIEALLDKFGGE HNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVTSSSSSSLSVLPSSLSVFQNP TDVARSNPKSPQKPIVRVFLPNKQRTVVPARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPIGWD TDISWLTGEELHVEVLENVPLTTHNFVRKTFFTLAFCDFCRKLLFQGFRCQTCGYKFHQRCSTEVPLMCV NYDQLDLLFVSKFFEHHPIPQEEASLAETALTSGSSPSAPASDSIGPQILTSPSPSKSIPIPQPFRPADE DHRNQFGQRDRSSSAPNVHINTIEPVNIDDLIRDQGFRGDGGSTTGLSATPPASLPGSLTNVKALQKSPG PQRERKSSSSSEDRNRMKTLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKWHGDVAVKMLNVTAPT PQQLQAFKNEVGVLRKTRHVNILLFMGYSTKPQLAIVTQWCEGSSLYHHLHIIETKFEMIKLIDIARQTA QGMDYLHAKSIIHRDLKSNNIFLHEDLTVKIGDFGLATVKSRWSGSHQFEQLSGSILWMAPEVIRMQDKN PYSFQSDVYAFGIVLYELMTGQLPYSNINNRDQIIFMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKKR DERPLFPQILASIELLARSLPKIHRSASEPSLNRAGFQTEDFSLYACASPKTPIQAGGYGAFPVH

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>gi|18497290|ref|NP_084056.1| protein kinase raf 1; murine sarcoma 3611
oncogene 1; sarcoma 3611 oncogene [Mus musculus]

>Mouse

MEHIQGAWKTISNGFGLKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTDSSKTSNTIRVFLPNKQRTVV NVRNGMSLHDCLMKALKVRGLQPECCAVFRLLQEHKGKKARLDWNTDAASLIGEELQVDFLDHVPLTTHN FARKTFLKLAFCDICQKFLLNGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNSTVGDSGVPAPP SFPMRRMRESVSRMPASSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVHMVSTTLHVDSRMIEDA IRSHSESASPSALSSSPNNLSPTGWSQPKTPVPAQRERAPGSGTQEKNKIRPRGQRDSSYYWEIEASEVM LSTRIGSGSFGTVYKGKWHGDVAVKILKVVDPTPEQLQAFRNEVAVLRKTRHVNILLFMGYMTKDNLAIV TQWCEGSSLYKHLHVQETKFQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLA TVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDDNPFSFQSDVYSYGIVLYELMAGELPYAHINNRDQIIFM VGRGYASPDLSRLYKNCPKAMKRLVADCVKKVKEERPLFPQILSSIELLQHSLPKINRSASEPSLHRAAH TEDINACTLTTSPRLPVF

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>gi|125653|sp|P11345|KRAF_RAT RAF proto-oncogene serine/threonine-protein kinase (RAF-1) (C-RAF)

>Rat.

MEHIQGAWKTISNGFGLKDAVFDGSSCISPTIVQQFGYQRRASDDGKLTDSSKTSNTIRVFLPNKQRTVV NVRNGMSLHDCLMKALKVRGLQPECCAVFRLLQEHKGKKARLDWNTDAASLIGEELQVDFLDHVPLTTHN FARKTFLKLAFCDICQKFLLNGFRCQTCGYKFHEHCSTKVPTMCVDWSNIRQLLLFPNSTASDSGVPAPP SFTMRRMRESVSRMPASSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVHMVSTTLPVDSRMIEDA IRSHSESASPSALSSSPNNLSPTGWSQPKTPVPAQRERAPGSGTQEKNKIRPRGQRDSSYYWEIEASEVM LSTRIGSGSFGTVYKGKWHGDVAVKILKVVDPTPEQLQAFRNEVAVLRKTRHVNILLFMGYMTKDNLAIV TQWCEGSSLYKHLHVQETKFQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGLTVKIGDFGLA TVKSRWSGSQQVEQPTGSVLWMAPEVIRMQDNNPFSFQSDVYSYGIVLYELMTGELPYSHINNRDQIIFM VGRGYASPDLSRLYKNCPKAMKRLVADCVKKVKEERPLFPQILSSIELLQHSLPKINRSASEPSLHRAAH TEDINACTLTTSPRLPVF

FIGURE 7C

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 $>gi|15227883|ref|NP_179361.1|$ putative protein kinase [Arabidopsis thaliana]

>Arabidopsis.

MTIKDESESCGSRAVVASPSQENPRHYRMKLDVYSEVLQRLQESNYEEATLPDFEDQLWLHFNRLPARYA LDVKVERAEDVLTHQRLLKLAADPATRPVFEVRSVQVSPRISADSDPAVEEDAQSSHQPSGPGVLAPPTF GSSPNFEAITQGSKIVEDVDSVVNATLSTRPMHEITFSTIDKPKLLSQLTSLLGELGLNIQEAHAFSTVD GFSLDVFVVDGWSQEETDGLRDALSKEILKLKDQPGSKQKSISFFEHDKSSNELIPACIEIPTDGTDEWE IDVTQLKIEKKVASGSYGDLHRGTYCSQEVAIKFLKPDRVNNEMLREFSQEVFIMRKVRHKNVVQFLGAC TRSPTLCIVTEFMARGSIYDFLHKQKCAFKLQTLLKVALDVAKGMSYLHQNNIIHRDLKTANLLMDEHGL VKVADFGVARVQIESGVMTAETGTYRWMAPEVIEHKPYNHKADVFSYAIVLWELLTGDIPYAFLTPLQAA VGVVQKGLRPKIPKKTHPKVKGLLERCWHQDPEQRPLFEEIIEMLQQIMKEVNVVV

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>gi|422343|pir||S33261 protein kinase lin-45 (EC 2.7.1.-) - Caenorhabditis elegans

>C elegans.

MSRINFKKSSASTTPTSPHCPSPRLISLPRCASSSIDRKDQASPMASPSTPLYPKHSDSLHSLSGHHSAG
GAGTSDKEPPKFKYKMIMVHLPFDQHSRVEVRPGETARDAISKLLKKRNITPQLCHVNASSDPKQESIEL
SLTMEEIASRLPGNELWVHSEYLNTVSSIKHAIVRRTFIPPKSCDVCNNPIWMMGFRCEFCQFKFHQRCS
SFAPLYCDLLQSVPKNEDLVKELFGIASQVEGPDRSVAEIVLANLAPTSGQSPAATPDSSHPDLTSIKRT
GGVKRHPMAVSPQNETSQLSPSGPYPRDRSSSAPNINAINDEATVQHNQRILDALEAQRLEEESRDKTGS
LLSTQARHRPHFQSGHILSGARMNRLHPLVDCTPLGSNSPSSTCSSPPGGLIGQPTLGQSPNVSGSTTSS
LVAAHLHTLPLTPPQSAPPQKISPGFFRNRSRSPGERLDAQRPRPPQKPHHEDWEILPNEFIIQYKVGSG
SFGTVYRGEFFGTVAIKKLNVVDPTPSQMAAFKNEVAVLKKTRHLNVLLFMGWVREPEIAIITQWCEGSS
LYRHIHVQEPRVEFEMGAIIDILKQVSLGMNYLHSKNIIHRDLKTNNIFLMDDMSTVKIGDFGLATVKTK
WTVNGGQQQQQPTGSILWMAPEVIRMQDDNPYTPQSDVYSFGICMYEILSSHLPYSNINNRDQILFMVGR
GYLRPDRSKIRHDTPKSMLKLYDNCIMFDRNERPVFGEVLERLRDIILPKLTRSQSAPNVLHLDSQYSVM
DAVMRSQMLSWSYIPPATAKTPQSAAAAAARNKKAYYNVYGLI

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>gi|17933524|ref|NP_525047.1| pole hole; pole-hole; raf-like-oncogene-1; 1(1)pole hole; Raf [Drosophila melanogaster]

>Drosophila.

MSSESSTEGDSDLYDPLAEELHNVQLVKHVTRENIDALNAKFANLQEPPAMYLIEYQELTSKLHELEAKE QELMERLNSQDQQEDSSLVERFKEQPHYQNQTQILQQQRQLARVHHGNDLTDSLGSQPGSQCGTLTRQPK ILLRAHLPNQQRTSVEVISGVRLCDALMKALKLRQLTPDMCEVSTTHSGRHIIPWHTDIGTLHVEEIFVR LLDKFPIRTHIKHQIIRKTFFSLVFCEGCRRLLFTGFYCSQCNFRFHQRCANRVPMLCQPFPMDSYYQLL LAENPDNGVGFPGRGTAVRFNMSSRSRSRCSSSGSSSSSKPPSSSSGNHRQGRPPRISQDDRSNSAPNV CINNIRSVTSEVQRSLIMQARPPLPHPCTDHSNSTQASPTSTLKHNRPRARSADESNKNLLLRDAKSSEE NWNILAEEILIGPRIGSGSFGTVYRAHWHGPVAVKTLNVKTPSPAQLQAFKNEVAMLKKTRHCNILLFMG CVSKPSLAIVTQWCEGSSLYKHVHVSETKFKLNTLIDIGRQVAQGMDYLHAKNIIHRDLKSNNIFLHEDL SVKIGDFGLATAKTRWSGEKQANQPTGSILWMAPEVIRMQELNPYSFQSDVYAFGIVMYELLAECLPYGH ISNKDQILFMVGRGLLRPDMSQVRSDAPQALKRLAEDCIKYTPKDRPLFRPLLNMLENMLRTLPKIHRSA SEPNLTQSQLQNDEFLYLPSPKTPVNFNNFQFFGSAGNI

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Human. Mouse.	MAALSGGGGGAEPGQALFNGDMEPEAGAGRPAASSAADPAIPEEVWNIKQMIKLTQEHI
Rat.	
Arabidopsis. C	M
Drosophila.	MSSESSTEGDSDLYDPLAEELHNVQLVKHVTRENI
Human.	EALLDKFGGEHNPPSIYLEAYEEYTSKLDALQQREQQLLESLGNGTDFSVSSSASMDTVT
Mouse. Rat.	MEHIQGAWKTISNGFGLKDAVF
Arabidopsis.	
C Drosophila.	SRINFKKSSASTTPTSPHCPSPRLISLPRCASSSIDRKDQAS DALNAKFANLQEPPAMYLIEYQELTSKLHELEAKEQELMERLNSQDQQEDSSLVERFKEQ
Human.	SSSSSSLSVLPSSLSVFQNPTDVARSNPKSPQKPIVRVFLPNKQRTVV
Mouse. Rat.	DGSSCISPTIVQQFGYQRRASDDGKLTDSSKTSNTIRVFLPNKQRTVV DGSSCISPTIVQQFGYQRRASDDGKLTDSSKTSNTIRVFLPNKQRTVV
Arabidopsis.	AVVASPSQENPRHYRM
C Drosophila.	PMASPSTPLYPKHSDSLHSLSGHHSAGGAGTSDKEPPKFKYKMIMVHLPFDQHSRV PHYQNQTQILQQQRQLARVHHGNDLTDSLGSQPGSQCGTLTRQPKILLRAHLPNQQRTSV
	. :: :
Human.	PARCGVTVRDSLKKALMMRGLIPECCAVYRIQDGEKKPIGWDTDISWLTGEELHV-
Mouse. Rat.	NVRNGMSLHDCLMKALKVRGLQPECCAVFRLLQ-EHKGKKARLDWNTDAASLIGEELQV- NVRNGMSLHDCLMKALKVRGLQPECCAVFRLLQ-EHKGKKARLDWNTDAASLIGEELQV-
Arabidopsis.	KLDVYSEVLQRLQESNYEEATLPDFEDQLWLHFNRLPARYALDVKVERAEDVLTH
C	EVRPGETARDAISKLLKKRNITPQLCHVNASSDPKQESIELSLTMEEIASRLPGNELWVH
Drosophila.	EVISGVRLCDALMKALKLRQLTPDMCEVSTTHSGRHIIPWHTDIGTLHVEEIFV- :::: *: ::::
Human.	-EVLENVPLTTHNFVRKTFFTLAFCDFCRK-LLFQGFRCQTCGYKFHQRCSTEVPLM
Mouse.	-DFLDHVPLTTHNFARKTFLKLAFCDICQK-FLLNGFRCQTCGYKFHEHCSTKVPTM
Rat. Arabidopsis.	-DFLDHVPLTTHNFARKTFLKLAFCDICQK-FLLNGFRCQTCGYKFHEHCSTKVPTM QRLLKLAADPATRPVFEVRSVQVSPRI-SADSDPAVEEDAQSSHQPSGPGVLAP
С	SEYLNTVSSIKHAIVRRTFIPPKSCDVCNNPIWMMGFRCEFCQFKFHQRCSSFAPLY
Drosophila.	-RLLDKFPIRTHIKHQIIRKTFFSLVFCEGCRR-LLFTGFYCSQCNFRFHQRCANRVPML * * * * * * * * * * * * * * * * * * *
Human.	CVNYDQLDLLFVSKFFEHHPIPQEEASLAETALTSGSSPSAPASDSIGP
Mouse. Rat.	CVDWSNIRQLLLFPNSTVGDSGVPAPPSFPMRRMRESVS CVDWSNIRQLLLFPNSTASDSGVPAPPSFTMRRMRESVS
Arabidopsis.	PTFGSSPNFE-AITQGSKIVEDVDSVVNATLSTRPMHEI
C Dragophile	COLLQSVPKNEDLVKELFGIAS-QVEGPDRSVAEIVLANLAPTSGQSPAATPDSSHP
Drosophila.	CQPFPMDSYYQLLLAENPDNGVGFPGRGTAVRFNM-SSRSRSR :
Human.	QILTSPSPSKSIPIPQPFRPADEDHRNQFGQRDRSSSAPNVH-INTIEPVNIDD-LI
Mouse. Rat.	RMPASSQHRYSTPHAFTFNTSSPSSEGSLSQRQRSTSTPNVHMVSTTLHVDSRM-IE RMPASSQHRYSTPHAFTFNTSSPSSEGSLSORORSTSTPNVHMVSTTLPVDSRM-IE
Arabidopsis.	TFSTIDKPKLLSQLTSLLGELGLNIQEAHAFSTVDGFSLDVFVVDGWSQEETDG-LR
C Decembéls	DLTSIKRTGGVKRHPMAVSPQNETSQLSPSGPYPRDRSSSAPNINAINDEATVQHNQRIL
Drosophila.	RCSSSGSSSSKPPSSSSGNHRQGRPPRISQDDRSNSAPNVC-INNIRSVTSEVQ : : :: :: :: ::
Human.	RDQGFRGDGGSTTG
Mouse.	DAIRSHSESASPSA
Rat.	DAIRSHSESASPSA
Arabidopsis. C	DALSKEILK DALEAQRLEEESRDKTGSLLSTQARHRPHFQSGHILSGARMNRLHPLVDCTPLGSNSPSS
Drosophila.	RSLIMQARPPLPHP
Human.	LSATPPASLPGSLTNVKALQKSPGPQRERKS
Mouse.	LSSSPNNLSPTGWSQPKTPVPAQRERAP
Rat.	LSSSPNQRERAP
Arabidopsis. C	LKDQPGFEHDK TCSSPPGGLIGQPTLGQSPNVSGSTTSSLVAAHLHTLPLTPPQSAPPQKISPGFFRNRSR
Drosophila.	CTDHSNSTQASPTSTLKHNRPRAR

 ${\tt SSSSEDRNRMKTLGRRDSSDDWEIPDGQITVGQRIGSGSFGTVYKGKW-HGDVAVKMLNV}$

Human.

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GSGTQEKNKIRPRGQRDSSYYWEIEASEVMLSTRIGSGSFGTVYKGKW-HGDVAVKILKV Mouse. Rat. GSGTQEKNKIRPRGQRDSSYYWEIEASEVMLSTRIGSGSFGTVYKGKW-HGDVAVKILKV Arabidopsis. SSNELIPA--CIEIPTDGTDEWEIDVTQLKIEKKVASGSYGDLHRGTYCSQEVAIKFLKP SPGERLDAQRPRPPQKPHHEDWEILPNEFIIQYKVGSGSFGTVYRGEF-FGTVAIKKLNV SADESNKN-LLLRDAKSSEENWNILAEEILIGPRIGSGSFGTVYRAHW-HGPVAVKTLNV Drosophila. :. : ::.***:* :::. : Human. TAPTPQQLQAFKNEVGVLRKTRHVNILLFMG-YSTKPQLAIVTQWCEGSSLYHHLHIIET Mouse. VDPTPEQLQAFRNEVAVLRKTRHVNILLFMG-YMTKDNLAIVTQWCEGSSLYKHLHVQET Rat. VDPTPEQLQAFRNEVAVLRKTRHVNILLFMG-YMTKDNLAIVTQWCEGSSLYKHLHVQET Arabidopsis. ${\tt DRVNNEMLREFSQEVFIMRKVRHKNVVQFLGACTRSPTLCIVTEFMARGSIYDFLHKQKC}$ VDPTPSQMAAFKNEVAVLKKTRHLNVLLFMG-WVREPEIAIITQWCEGSSLYRHIHVQEP Drosophila. KTPSPAQLQAFKNEVAMLKKTRHCNILLFMG-CVSKPSLAIVTQWCEGSSLYKHVHVSET * :** :::*.** *:: *:* :.*:*:: . * : * K--FEMIKLIDIARQTAQGMDYLHAKSIIHRDLKSNNIFLHEDL-TVKIGDFGLATVKSR Human. K--FQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGL-TVKIGDFGLATVKSR Mouse. K--FQMFQLIDIARQTAQGMDYLHAKNIIHRDMKSNNIFLHEGL-TVKIGDFGLATVKSR Rat. A--FKLQTLLKVALDVAKGMSYLHQNNIIHRDLKTANLLMDEHG-LVKVADFGVARVQIE Arabidopsis. RVEFEMGAIIDILKQVSLGMNYLHSKNIIHRDLKTNNIFLMDDMSTVKIGDFGLATVKTK Drosophila. K--FKLNTLIDIGRQVAQGMDYLHAKNIIHRDLKSNNIFLHEDL-SVKIGDFGLATAKTR ::.: ::: **.*** :.****:*: *::: : WS--GSHQFEQLSGSILWMAPEVIRMQDKNPYSFQSDVYAFGIVLYELMTGQLPYSNINN Human. Mouse. WS--GSQQVEQPTGSVLWMAPEVIRMQDDNPFSFQSDVYSYGIVLYELMAGELPYAHINN WS--GSQQVEQPTGSVLWMAPEVIRMQDNNPFSFQSDVYSYGIVLYELMTGELPYSHINN Rat. SG----VMTAETGTYRWMAPEVIEH---KPYNHKADVFSYAIVLWELLTGDIPYAFLTP Arabidopsis. WTVNGGQQQQPTGSILWMAPEVIRMQDDNPYTPQSDVYSFGICMYEILSSHLPYSNINN WS--GEKQANQPTGSILWMAPEVIRMQELNPYSFQSDVYAFGIVMYELLAECLPYGHISN Drosophila. ******. :*:. ::**:::.* ::*::: RDOIIFMVGRGYLSPDLSKVRSNCPKAMKRLMAECLKKKRDERPLFPOILASIELLARSL Human. RDQIIFMVGRGYASPDLSRLYKNCPKAMKRLVADCVKKVKEERPLFPQILSSIELLQHSL Mouse. RDOIIFMVGRGYASPDLSRLYKNCPKAMKRLVADCVKKVKEERPLFPOILSSIELLOHSL Rat. LQAAVGVVQKGL----RPKIPKKTHPKVKGLLERCWHQDPEQRPLFEEIIEMLQQIM---Arabidopsis. RDQILFMVGRGYLRPDRSKIRHDTPKSMLKLYDNCIMFDRNERPVFGEVLERLRDII--L Drosophila. $\verb"KDQILFMVGRGLLRPDMSQVRSDAPQALKRLAEDCIKYTPKDRPLFRPLLNMLENMLRTL"$.:: . .:**:* Human. PKIHRSASEPSLNRAGFQTEDFSL-----YACASPKTPIQAGGYGAFPVH----PKINRSASEPSLHRAAHTEDINAC-----TLTTSPRLPVF-----Mouse. PKINRSASEPSLHRAAHTEDINAC-----TLTTSPRLPVF------Rat. KEVNVVV-----Arabidopsis. PKLTRSQSAPNVLHLDSQYSVMDAVMRSQMLSWSYIPPATAKTPQSAAAAAARNKKAYYN Drosophila. PKIHRSASEPNLTQSQLQNDEF-----LYLPSPKTPVNFNNFQFFGSAGNI-Human. ----Mouse. --------Arabidopsis. ____ VYGLI Drosophila.

MELANOMA AND TREATMENTS THEREOF

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